FACTORS CONTROLLING THE INTESTINAL BACTERIA

THE EFFECT OF ACUTE OBSTRUCTION AND STASIS ON BACTERIAL TYPES

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The demonstration of the rôle played by intestinal bacteria in the toxemia of intestinal obstruction as developed by the authors [1] and the great probability of the importance of these organisms in other pathologic conditions makes it of considerable practical as well as theoretical importance to determine all of the factors which influence the types of intestinal flora. Kendall's [2] recent researches have indicated brilliant therapeutic possibilities in specific infections of the gastro-intestinal tract which depend on the adequate control of either the types of intestinal bacteria or of their metabolic processes. The work of Kendall,[2] Hull and Rettger,[3] Torrey,[4] Cannon,[5] Rettger and Cheplin [6] and others has demonstrated that the types of intestinal bacteria depend to a great extent on the character of the diet. A diet rich in protein of animal origin brings about an intestinal flora dominated by proteolytic putrefactive organisms, while a carbohydrate diet, more particularly one containing definite amounts of either lactose or dextrin, produces a complete change in the intestinal bacteria so that the predominant organisms are fermentative or aciduric. Apparently many recent workers have lost sight of the more significant fact pointed out by Kendall that not only is a change in the types of bacteria effected by diet but also a change in their metabolism as determined by an analysis of the end products of their activity, in the one case when they must obtain their energy solely from protein and in the other when a readily utilizable carbohydrate is present.

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[1] Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: Jour. Exper. Med., 1917, 25, p. 421. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Ibid., 1919, 30, p. 109. Dragstedt, C. A.; Dragstedt, L. R., and Chase, C. S.: Am. Jour. Physiol, 1918, 46, p. 366. Dragstedt, C. A., and Moorhead, J. J.: Jour. Exper. Med., 1918, 27, p 359.

[2] Am. Jour. Med. Sc., 1918, 156, p. 157.

[3] Jour. Bacteriol., 1917, 2, p. 47.

[4] Jour Med. Res., 1919, 39, p. 415.

[5] Jour. Infect. Dis., 1920, 27, p. 139 and 1921, 29, p. 369.

[6] Transformation of the Intestinal Flora, 1921.

It is the general view that the addition of lactose or dextrin to the diet brings about the change in the intestinal types because these carbohydrates, unlike others, are slowly absorbed and hence reach the region of maximum bacterial activity. Under these conditions it would seem that the suppression of proteolytic organisms, which grow best in a slightly alkaline medium, would be due to the accumulation of acid metabolites and the consequent change in the reaction of the medium. The aciduric bacteria, on the other hand, apparently prefer a slightly acid medium, and so would find conditions for their growth more favorable. Kendall maintains that when even small amounts of carbohydrates are present the proteolytic organisms obtain their energy from this source, and their metabolites are now acid in nature. These observations would suggest that with carbohydrate feeding both the aciduric and proeolytic organisms combine to form a medium favorable for the former and unfavorable for the latter. This interpretation is in accord with the well-known observation that the feces of the breast-fed infant are acid in reaction whereas those of an adult on a high animal protein diet are alkaline, and coincides with the facts in the natural souring of milk and the ripening of silage, where the evidence is convincing that the first stage is carried on by members of the colon-aerogenes group, and as the acidity increases these are out-numbered by streptococci and these in turn by lactobacilli.

Rettger and Cheplin, however, have found no relation between acidity of the feces and the presence of B. acidophilus, and they interpret the predominance of B. acidophilus as being the result of optimum cultural and environmental conditions for the development of members of the aciduric group. Whatever may be the exact factor in determining the predominance of types, it is apparent that diet is not the sole factor, as the bacteria are subjected to all the variations in functions of the intestinal tract, namely, motility, secretions, and degree of absorption.

EFFECT OF OBSTRUCTION ON BACTERIAL TYPES

We have previously reported experiments in lower animals in which the evidence seemed to prove that the toxemia of acute intestinal obstruction is directly dependent on the nature of the intestinal flora. The accompanying table includes the results of these experiments together with those of 2 more groups (groups 4 and 5) studied later. White rats were used and were divided into 2 groups, one being fed a meat diet and one a meat and lactose diet. Under these conditions

the undigested residues were more nearly comparable than in the preceding experiments. The diets were given for one week, and at the end of this time fresh feces of the animals were plated, and the results expressed in terms of the proportion of B. coli to B. acidophilus as the C-A ratio (Cannon [5].) A complete obstruction in the lower colon was then produced by ligation with tapes. The diets were continued after the operation. All of the animals in which the obstruction remained complete died within 11 days and at necropsy an examination was made of the intestinal flora above the obstruction. The results are shown in the table.

It will be seen that the animals whose intestinal flora was aciduric survive the obstruction a little longer than those whose flora was proteolytic. There was, however, a much more marked difference in the postoperative behavior of these two groups. The meat eaters were listless

TABLE 1

RESULTS OF NECROPSY EXAMINATION

Groups	No. of Rats	Diet	C-A Ratio (Average)	Days Survived Obstruction	C-A Ratio After Death
1	3	Stock diet: oats, cabbage, carrots..	3 : 97	6½	90-10
2	15	Meat diet: ground beef, cabbage, carrots.....	87 : 13	7½	99 : 1
3	12	Lactose diet: whole milk, whole wheat bread, lactose, cabbage....	2 : 98	9½	97 : 3
4	4	Meat diet: ground beef.....	99 : 1	6	99 : 1
5	4	Lactose diet: ground beef 7 parts, lactose 3 parts.....	1 : 99	10½	98 : 2

from the first and refused their food. The lactose eaters, on the other hand, were alert and always eager for food. This is confirmatory of the conclusions of two of us in regard to the nature of the toxic substances in acute intestinal obstruction, namely, that they are produced by the activity of proteolytic intestinal organisms. The postoperative behavior of the meat eaters is also very similar to that of the monkey studied by Herter and Kendall [7] which was sleepy and stupid when being fed a diet encouraging the growth of proteolytic organisms, but became alert when carbohydrates were added to the diet. More recently Underhill and Simpson [8] have observed similar effects in a dog fed the two types of diet. The striking thing about these experiments, however, is that irrespective of the character of the diet, i. e., whether lactose is given or not, a complete stasis of the intestinal content results in a proteolytic intestinal flora.

[7] Jour. Biol. Chem., 1908, 7, p. 203.
[8] Ibid., 1920, 44, p. 90.

The results obtained in rats were entirely confirmed in dogs. Young animals were selected for this work and, confirming the observations of Torrey, it was found that diets of bread, milk, and lactose, or boiled rice, beef heart, and lactose in definite amounts would produce in these animals an aciduric intestinal flora. On the other hand, a diet of meat alone or of meat and boiled rice would develop a proteolytic flora. A complete obstruction was then produced in the transverse colon by section and closure of the divided ends. Following the operation the animals were kept on their respective diets. All of them died in the course of 2 weeks, those fed on the lactose surviving 2 or 3 days longer on the average than the meat eaters. At necropsy in all cases there was found above the site of obstruction a foul smelling, dark gray fluid, and examination revealed a great predominance of gram-negative proteolytic organisms.

BACTERIAL TYPES IN CLOSED INTESTINAL LOOPS

It has been demonstrated [1] that when closed isolated intestinal segments are made in dogs, the animal usually dies in 4 to 5 days of an acute toxemia developing from the isolated loop. The responsible toxic substances in the loop contents belong to the class of amines, and the rapid distention of the loop by the enclosed secretions so injures the intestinal wall that they are rapidly absorbed unchanged into the blood stream. Bacteriologic examination of the loop fluid from dogs which have previous to the operation been fed on the regular stock diet, shows a great preponderance of gram-negative organisms. The same is true of animals that have been fed meat previous to the production of the closed loop.

In these experiments isolated segments of the small intestine of dogs were made by cutting the intestine across in two places approximately 12 inches apart and then reestablishing the continuity of the alimentary tract by anastomosing the proximal and distal ends of the cut intestine. The isolated segments with intact mesentery were then closed at both ends and returned to the abdominal cavity. The operations were performed with aseptic precautions. Previous to the operation the dogs were fed either on a diet of bread, milk, and lactose, or boiled rice, beef heart, and lactose, and in each case the fecal flora was found to be strongly aciduric. At operation smears from the jejunal content revealed gram-positive organisms chiefly. These animals did not survive the production of a closed intestinal loop any longer than dogs fed on a meat diet. In every case at death the bacteria

in the closed loops were almost entirely gram-negative in type. This point was noted by Reynolds and McClintock.[9] The loop fluid was alkaline to litmus.

Isolated closed intestinal loops previously washed with ether and sterile water usually show in 4 or 5 days an accumulation of great numbers of gram-negative organisms. These apparently live in the intestinal secretions, and the medium does not inhibit their growth. If isolated intestinal loops are washed with a saturated solution of tannic acid previous to closure, their distention and the consequent production of a toxemia is prevented. Animals may survive indefinitely with such closed intestinal segments. The loop contents examined after from several months to a year still show great numbers of viable gram-negative organisms. Apparently the succus entericus is not sufficiently bactericidal to suppress the growth of these organisms and is not comparable to the fluid in the free abdominal cavity in that respect. It is probable that the gram-positive bacteria disappear from these loops for the same reasons that they disappear from the normal intestine in starvation.

EFFECT OF STASIS ON BACTERIAL TYPES

An attempt to secure a slowing of the intestinal current without complete obstruction was not very successful. The best of the methods used was the isolation and inversion of an intestinal segment in the manner described by Mall.[10] In 2 dogs an aciduric intestinal flora was produced by a diet of bread, milk, and lactose. Isolated segments of the intestine 12 inches in length were produced and then stitched back into place in the inverted position. It was assumed in accordance with the usual view of intestinal peristalsis that when the intestinal content would encounter this reversed segment a stasis would result unless the material could be mechanically squeezed through. Our results corroborated the findings of Beer and Eggers [11] and McClure and Derge [12] rather than those of Mall. There was evidence of an obstruction, with vomiting and loss of appetite lasting for a week or two, but thereafter the animal was active, had a good appetite and regular bowel movements. During the period of obstructive symptoms the fecal material was scant, and there was a tendency for the gram-

[9] Personal communication.
[10] Johns Hopkins Hospital Reports, 1896, 1, p. 93.
[11] Annals of Surgery, 1907, 46, p. 576.
[12] Bull. Johns Hopkins Hospital, 1907, 18, p. 472.

positive organisms to be replaced by gram-negative bacteria. When the obstructive symptoms disappeared and the bowel movements became regular the aciduric bacteria once more gained the ascendancy. The significance of this experiment is lessened because during the period of obstructive symptoms it was difficult to get the animals to retain the food.

DISCUSSION

Evidence is presented which indicates that other factors than the character of the diet are concerned in determining the type of intestinal flora. Either a complete obstruction or a stasis in the passage of the intestinal content results in a proteolytic flora irrespective of the character of the diet. It is probable, however, that the mechanism of bacterial control is identical in both cases and is dependent on the presence of utilizable carbohydrate in all parts of the small intestine and colon. In conditions of stasis or obstruction even such carbohydrates as dextrin and lactose are probably completely absorbed in the upper part of the intestine and so cannot affect bacterial growth lower down.

The experiments with the closed intestinal loops demonstrate that the intestinal juice is not markedly bactericidal, at least so far as the proteolytic group of organisms is concerned. The disappearance of the gram-positive aciduric bacteria is probably due to the fact that carbohydrates are absent from such loops and that the intestinal juice is quite markedly alkaline in reaction.

CONCLUSIONS

Intestinal stasis or complete obstruction leads to the development of a proteolytic intestinal flora irrespective of the character of the diet.

The intestinal secretions do not suppress the growth of gram-negative bacteria in closed intestinal loops.

The disappearance of gram-positive aciduric organisms from closed intestinal loops is probably due to the absence of utilizable carbohydrate and to the alkaline reaction of the medium.